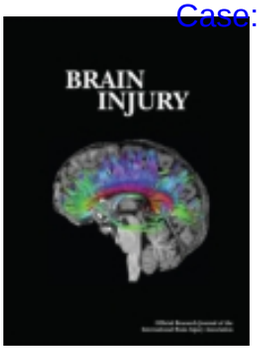

Taylor & Francis
Taylor & Francis Group

Brain Injury

ISSN: 0269-9052 (Print) 1362-301X (Online) Journal homepage: http://www.tandfonline.com/loi/ibij20

A systematic review of age and gender factors in prolonged post-concussion symptoms after mild head injury

Nigel S. King

To cite this article: Nigel S. King (2014) A systematic review of age and gender factors in prolonged post-concussion symptoms after mild head injury, Brain Injury, 28:13-14, 1639-1645, DOI: 10.3109/02699052.2014.954271

To link to this article: http://dx.doi.org/10.3109/02699052.2014.954271

BRAIN INJURY

http://informahealthcare.com/bij
ISSN: 0269-9052 (print), 1362-301X (electronic)

Brain Inj, 2014; 28(13–14): 1639–1645
 DOI: 10.3109/02699052.2014.954271

informa
healthcare

REVIEW

A systematic review of age and gender factors in prolonged post-concussion symptoms after mild head injury

Nigel S. King[1,2]

[1]Community Head Injury Service, The Camborne Centre, Aylesbury, Bucks, UK and [2]The Oxford Institute for Clinical Psychology Training, University of Oxford, Warneford Hospital, Oxford, UK

Abstract

Background: Older age and female gender are known factors in the development of persisting post-concussion symptoms (PCS) after mild head injury (MHI), i.e. at 3+ months. Very few studies have examined longer-term symptoms. A recent review, however, established the importance of these variables in permanent PCS (18+ months). The current study repeats the review for prolonged symptoms (12–18 months).

Methods: Systematic electronic database searches were conducted to identify all studies with data on (i) correlations between age/gender and prolonged outcome and (ii) mean ages/gender mixes of (a) prolonged samples selected for poor symptomatic outcome, (b) prolonged samples not selected for poor outcome and (c) epidemiological studies of MHI patients presenting to hospital.

Results: Correlation studies showed poorer outcome to be associated with both older age (2/5 studies) and female gender (5/6 studies). Those with poor prolonged outcome had a significantly higher mean age (35.9) than MHI patients in general (29.9). The proportion of men in these samples (48.6%) was significantly lower than MHI patients in general (66.7%).

Conclusions: Older age and female gender are vulnerability factors in the development of prolonged PCS. The main clinical implications are for how early intervention and reassurance are best provided.

Keywords

Mild head injury, prolonged post-concussion symptoms

History

Received 13 December 2013
Revised 8 August 2014
Accepted 10 August 2014
Published online 29 September 2014

Introduction

Mild head injury (MHI) is usually defined as a trauma to the head resulting in post-traumatic amnesia (PTA) of less than 24 hours, GCS of 13–15 and no evidence of intracranial abnormality on CT [1]. In developed countries such injuries are very common and approximately half of those who sustain one experience post-concussion symptoms (PCS) [2,3]. These are a cluster of cognitive, somatic and emotional symptoms caused by neuropathological and/or psychological mechanisms which are poorly understood [4]. They include headaches, dizziness, fatigue, irritability, reduced concentration, sleep disturbance, memory dysfunction, sensitivity to light or noise, double or blurred vision, frustration, restlessness, anxiety, depression, tinnitus and sensitively to alcohol [4]. They fully resolve within 3 months for the vast majority [5] and some have put this figure at ~80% [6]. A minority, however, have more chronic symptoms and a small minority experience permanent PCS [7]. There is no agreed terminology regarding the ongoing experience of these symptoms. Terms such as 'persisting', 'chronic', 'long-term' and 'late' are inconsistently used to describe symptoms that last from 1 month to many years [7–9]. Previous papers have argued that the term 'permanent' could reasonably be applied to symptoms lasting 18 months and beyond, as this is broadly the period within which maximum neuronal healing occurs in severe head injuries [7, 10]. The term 'persisting' is used very inconsistently and has described the occurrence of PCS from anywhere between 1 month to 4 years [9]. It is, therefore, proposed that, for the purposes of this paper, symptoms persisting for 12–18 months be termed 'prolonged'.

It should also be noted that the MHI population is very heterogeneous and outcome is not predicted well by either PTA or GCS [1, 11, 12]. A wide range of factors outside of the MHI can significantly affect the severity and chronicity of PCS. These include concurrent factors such as pain, anxiety, depression, post-traumatic stress and litigation [5]. They also include pre-injury variables such as pre-morbid: psychopathology; substance misuse; MHIs; and other forms of acquired brain injury [5]. More recently, a number of biomarkers have shown some promise in the prediction of longer-term outcome in more severe head injuries and in the diagnosis of MHI [13]. These include specific proteins that are released after injury like S100B, Neuron Specific Enolase (NSE) and

Correspondence: Dr. Nigel King, Bsc, Clin PsyD, CPsychol, The Oxford Institute for Clinical Psychology Training, University of Oxford, Warneford Hospital, Oxford OX3 7JX, UK. Tel: 01865 226431. Fax: 01865 226364. Email: nigel.king@hmc.ox.ac.uk

Cleaved-Tau Protein. Currently, S100B appears to show the most promise as a potential screening tool for identifying MHI [14]. Unfortunately, longitudinal studies of biomarker levels in patients with clinically relevant MHI are scarce [13]. Predicting outcome with biomarkers is, therefore, still very limited.

Newer and more sensitive imaging modalities like Diffuse Tensor Imaging (DTI) have also shown promise in identifying MHI and in predicting longer-term outcome. DTI studies have demonstrated damage to neural tracts in the internal capsule, corpus callosum and subcortical white matter areas in patients with MHI up to 4 years post-injury [15, 16]. The resolution of such damaged areas has also been shown to correlate with neuropsychological deficits and their resolution, over the first 6 months of injury [17]. Whilst such studies have yielded quite consistent results in the acute and sub-acute phases, the results are less reliable for the more chronic phases [18].

Two other factors that have been implicated in poorer outcome, at least in the initial stages after MHI, are female gender and older age [5]. There is evidence that in severe head injuries a degree of neuroprotection may be afforded by some of the female sex hormones, particularly progesterone [19]. The data in this area, however, are by no means consistent and some studies have demonstrated better neuropsychological outcome in women, while others have shown better functional outcome in men [19]. In MHI, however, female gender is more associated with poorer initial outcome, although findings in this area are also quite mixed [5]. Poorer initial outcome with increased age is a more consistent finding with a tendency for children to have better outcomes than adults, adults under 40 to have better outcomes than those over 40 and working-age adults to have better outcomes than Older Adults (over 65) [5]. Therefore, increased age (with a putative cut-off $>$ 40 years) and female gender have, for some time now, been associated with an initial increased risk of PCS [20]. Until recently their role in prolonged or permanent PCS was implied from this data but had not been established empirically.

A recent systematic literature review, however, examined gender and age factors in working-age patients with permanent symptoms [21]. It identified and summarized studies which had examined correlations between permanent PCS and age or gender. It also compared the mean ages and gender ratios of cohorts selected for poor long-term outcome with those not selected for such and with MHI populations in general [21]. It showed positive correlations in three out of four studies examining the relationship between older age and permanent PCS. It also showed that the mean age of patients selected for poor symptomatic long-term outcome (40.6 years) was significantly higher than those not selected for poor outcome (32.5 years). In addition, it showed it was higher than in patients with MHI of working-age in general (29.9 years). In addition, it revealed that: (i) there were positive correlations in two out of four studies examining the relationship between female gender and permanent PCS, (ii) the mean proportion of women in groups selected for poor symptomatic outcome was significantly higher (55.2%) than in those not selected for poor outcome (33.5%) and (iii) this proportion was also higher in patients with MHI of working-age in general (33.3%). It, therefore, provided empirical evidence that older age and female gender may be significant vulnerability factors in the development of permanent PCS in adults.

Such findings have helped the conceptualization of PCS. The positive relationship between increased age and poorer outcome has often been taken as indirect evidence for the potential long-term role of neurogenic factors in PCS, at least for some patients [10]. The phenomenon is taken to reflect the slower and less complete healing processes that occur with older age in many biological systems. Psychological factors, however, cannot be excluded from explaining this finding as there is at least some evidence of a relationship between older age and increased psychopathology in working-age populations [22]. The role of female gender has often been taken as indirect evidence of psychological factors in PCS as women generally present more frequently with mental health problems than men [22]. Others, however, have speculated that there may be gender differences in the neuroanatomical reactions to mild head trauma which might equally explain such findings [21]. The findings, nonetheless, are useful clinically, particularly with regards to information giving and psychoeducation. These are often pivotal components of early intervention. Knowing which patients are more likely to ultimately experience longer-term PCS means that more flexible and guarded prognostic information can be provided to them. This is likely to help the maintenance of clinical credibility and effective therapeutic relationships over time.

These permanent PCS findings have not been established for prolonged symptoms. Therefore, to further examine the robustness of the role of these factors in chronic PCS, the original review was repeated for prolonged PCS, i.e. at 12–18 months.

This paper, therefore, systematically reviews the literature to identify and examine those studies which have investigated working-age patients with prolonged PCS (i.e. at 12–18 months post-injury). It summarizes the results of all studies which have examined the relationship between age or gender and prolonged symptoms. It also compares the overall mean ages and gender mixes of samples selected for poor prolonged symptomatic outcome with groups not selected for poor outcome. In addition, it compares these means with the epidemiological data of working-age patients presenting to hospital with MHI. The review restricted itself to working-age patients (16–65 years) due to the confounding variables of developmental factors in children and the higher prevalence of additional health difficulties in older adults. It should be acknowledged, however, that there are increased risks of MHI in both of these groups [23].

Methods

The sources of literature for the systematic review were: Medline 1966–, Embase 1966–, Cinahl 1980– and Psych INFO 1805– to the end of May 2011. Articles in these databases are largely indexed under thesaurus terms. The search used two main exploded thesaurus terms—‘Brain Concussion’ (exp BRAIN CONCUSSION below) and ‘Post-concussion Syndrome’ (exp POST-CONCUSSION

DOI: 10.3109/02699052.2014.954271

SYNDROME below). The scoping definition for the former was:

A non-specific term used to describe transient alterations or loss of consciousness following closed head injuries. Concussions may be classified as mild, intermediate or severe. The duration of unconsciousness generally lasts a few seconds, but may persist for several hours. Prolonged periods of unconsciousness (often defined as greater than 6 hours in duration) may be referred to as post-traumatic coma.

The exploded term included 'concussion' and 'cerebral concussion' in its indexing definition. The scoping definition of the latter was:

The organic and psychogenic disturbances observed after closed head injuries. Post-concussion syndrome includes subjective physical complaints (i.e. headache, dizziness), cognitive, emotional and behavioural changes. These disturbances can be chronic, permanent or late emerging.

This included 'post-concussion symptoms' and 'post-concussive symptoms' in its indexing definition. Combined with these indexed-based searches, free text searches were used to additionally identify key words in titles or abstracts for all the lower case terms and abbreviations below.

The search strategy was:

(1) exp BRAIN CONCUSSION,
(2) exp POST- CONCUSSION SYNDROME,
(3) 'mild traumatic brain injury'.ti,ab,
(4) 'mild TBI'.ti,ab,
(5) 'MTBI'.ti.ab,
(6) 'mild head'.ti.ab.
(7) 'brain concuss*'.ti.ab,
(8) 'brain contus*'.ti.ab,
(9) 1 OR 2 OR 3 OR 4 OR 5 OR 6 OR 7 OR 8,
(10) 'persist*'.ti,ab,
(11) 'long term'.ti.ab,
(12) 'longterm'.ti,ab,
(13) 'permanen*'.ti,ab,
(14) 'prolong*'.ti.ab,
(15) 'late recover*'.ti,ab,
(16) 'poor outcome*'.ti,ab,
(17) 'disabl*'.ti,ab,
(18) 'acute'.ti,ab,
(19) exp TIME FACTORS,
(20) exp FOLLOW-UP STUDIES,
(21) 10 OR 11 OR 12 OR 13 OR 14 OR 15 OR 16 OR 17 OR 18 OR 19 OR 20,
(22) exp ADULT, and
(23) 9 AND 21 AND 22.

The combination of these expanded thesaurus terms alongside the secondary free text terms enabled the search to include all major and minor terminologies used for the papers relevant to the review.

Full papers were examined of all abstracts obtained from the searches which appeared to fulfil the following inclusion and exclusion criteria: Inclusion criteria; injuries associated with GCS 13–15 and/or PTA less than 24 hours and/or loss of consciousness less than 6 hours, mean time post-injury of 12–18 months (the operational definition of 'prolonged'), minimum sample size of six, injuries sustained between 16–65 years old, data reported on the relationship between age or gender and prolonged outcome, data reported on the mean age or gender mix of any prolonged sample, English language: Exclusion criteria; samples with artificially restricted age ranges or gender mix (e.g. college or military cohorts), samples where age or gender data was reported for less than 75% of the subjects, letters to editors and editorials. Studies referenced in the examined literature which appeared to fall within the criteria were also scrutinized for inclusion, even if they fell outside the electronic searches.

To obtain MHI epidemiological data a similar search was conducted where the exploded thesaurus term 'exp EPIDEMIOLOGY' and free text term 'epidemiolog*.ti,ab' were substituted for the 'exp ADULT' term from the first search. All studies reporting data on the age or gender mix of patients presenting to hospital with MHI were included if they fulfilled the additional criteria of being (i) MHI epidemiological studies; (ii) epidemiological studies of head injury where the vast majority had MHI; or (iii) large scale MHI studies with representative samples of $n > 300$.

Results

In total, 1341 abstracts were identified by the electronic searches and 77 full papers were subsequently analysed. Sixteen fulfilled the inclusion and exclusion criteria. Six had correlation data for age or gender and prolonged PCS. These are presented in Table I.

Ten studies had age and gender data for samples either selected or not selected for poor prolonged outcome. These are presented in Table II.

Table III shows the combined mean ages for the prolonged PCS samples, alongside the same combined data for the permanent PCS groups from the previous literature review [21]. It also displays the same data for the five epidemiological or large scale studies obtained which reported mean age [38–42]. Three of the latter provided standard deviation data which allowed for comparisons with the other groups.

Table IV shows the combined proportion of men in the prolonged PCS samples alongside the same combined data for the permanent PCS samples from the previous literature review [21]. It also displays the same data for the eight epidemiological or large sample studies obtained which reported gender ratios [23, 38–44].

Table I shows that there were five studies which reported correlation data on age and symptomatic outcome. One showed a positive correlation between older age and poorer outcome at $p < 0.05$, one showed a positive correlation at $p < 0.06$ and three showed no correlation. No studies found a negative correlation. Table III shows that the mean age of the patients selected for poor prolonged outcome was 35.9 years. Using *t*-tests and simple Bonferroni corrections, this is very significantly higher than the mean age of patients with MHI of working-age presenting at hospital (29.9, $p < 0.0005$). It is not significantly different to patients not selected for poor outcome at 12–18 months (36.2). It is significantly lower than those selected for poor outcome at 18+ months (40.6, $p < 0.0001$), but not significantly different to those not selected for poor outcome at 18+ months (32.5).

Table I also shows that there were six studies which reported correlation data on gender and outcome. Five reported a positive correlation between female gender and

Table I. Studies with correlations between age/gender and prolonged PCS.

	n	Mean time post-injury, years	Mean age (SD)	Older age correlated to poorer outcome?	% men	Female gender correlated to poorer outcome?	Type of study	Population	Comments
Rutherford et al. [20]	131	1	No data	Yes at $p<0.06$ (but not at $p<0.05$)	63%	Yes	PCS Prevalence study	Unselected group of consecutively admitted MHI patients to an observation ward	Concluded that it would be surprising if a larger sample did not confirm association between older age PCS severity
Middleboe et al. [24]	28	1	No data; median = 37.0	No	54%	No	Prospective study of MHI patients admitted to a Neurology Department of a single hospital	Unselected consecutive MHI patients	
Alves et al. [25]	189 (from a sample of 587)	1	No data; Mode = 20–29 y.o.*	No	67%	Yes	Prevalence study of persisting PCS following MHI	Unselected group of consecutively admitted MHI patients	*2.9% of the original sample were older than 69 years
Thornhill et al. [26]	362	1	No data*	Yes	79%	Yes	Prospective study of 'poor outcome & death' following MHI	Unselected group of consecutively admitted MHI patients	*Included patients ≥14 years old
Mickeviciene et al. [27]	192 (from a sample of 217)	1	34.7 (13.5) (of the $n=217$)	No	66% (of the $n=217$)	Yes	Prospective follow-up study of MHI patients seen in two Emergency Wards	Unselected prospective MHI group	
Slatyer et al. [28]	728	>1	No data	No data	No data	Yes	Explorative study involving multi-domain follow-up of all MHI patients seen in an Emergency Department	Unselected cohort of all MHI patients seen in Accident and Emergency in Southern Tasmania	Initial findings published in abstract only

DOI: 10.3109/02699052.2014.954271

Table II. Studies with age/gender data and prolonged PCS.

	n	Mean time post-injury, years;months	Mean age (SD)	% men	Population
Cicerone et al. [29]	37 (from a sample of 50)	1;2 (0;3–4;4)	36.5 (10.8) (of the $n = 50$)	38%	Selected patients with persisting PCS
Kant et al. [9]	43	1;4 (0;1–5;4)	34.9 (No data)	72%	Selected patients with ongoing neuropsychiatric problems
Paniak et al. [30]	105	1	33.2 (12.2)	46%	Non-selected MHI patients admitted to two Emergency Wards
Hartlage et al. [31]	70	1	35 (No data)	45%	Selected group of consecutive patients with persisting neuro-behavioural problems referred for neuropsychological assessment. All involved in litigation
Emanuelson et al. [32]	101	1	31.7 (11.9)	65%	Non-selected consecutive MHI patients
Goranson et al. [33]	42	1	35.6 (12.5)	40%	Selected patients referred for treatment at an outpatient head injury clinic
Heitger et al. [34]	37	1	29.1 (12.7)	65%	Non-selected MHI patients
Stalnacke et al. [35]	16 (from original study sample of 69)	1;3	No data	44%	Selected MHI patients with persisting PCS seeking a follow-up consultation (from 69 consecutive patients originally admitted for observation)
de Leon et al. [36]	231	1	41.1 (No data)	42%	Non-selected group of MHI patients presenting at a single hospital
Roe et al. [37]	52	1	39.0 (12.0)	62%	Non-selected patients admitted to a single neurosurgical department

Table III. Mean ages of the combined samples.

Sample	Mean age	SD	Number in combined sample
Selected for poor outcome at 12 months	35.9 (35.4)	11.9	107 (220)
Non-selected at 12 months	36.2	15.3	718
Epidemiological studies	29.9 (30.5)	14.6	2317 (5212)
Selected for poor outcome at 18+ months [21]	40.6	10.0	289
Non-selected at 18+ months [21]	32.5 (32.4)	10.2	111 (632)

(Mean ages and combined sample numbers when samples which did not report standard deviations are also included (but which, therefore, could not be used in statistical analyses).

Table IV. Percentages of men in the combined samples.

Sample	Percentage of men	Number in combined sample
Selected for poor outcome at 12 months	48.6	208
Non-selected at 12 months	63.4	1428
Epidemiological studies	66.7	12070
Selected for poor outcome at 18+ months [21]	54.8	281
Non-selected at 18+ months [21]	66.5	1273

poorer symptomatic outcome and one found no correlation (the smallest study). No studies found a negative correlation. Table IV shows that the proportion of men in prolonged PCS studies with patients selected for poor outcome was 48.6%. Using *t*-tests with simple Bonferroni corrections this is significantly lower ($p < 0.0001$) than those studies not selected for poor prolonged outcome (63.4%). It is also significantly lower than for those not selected for poor outcome at 18+ months (66.5, $p < 0.0001$) and for patients with MHI of working-age presenting at hospital (66.7, $p < 0.0001$). It is not significantly different to the group selected for poor outcome at 18+ months (54.8).

Discussion

The review provides evidence that older age is associated with poorer symptomatic outcome at 12–18 months after a MHI. Two out of five studies found a positive correlation between these factors and none found a negative one. Also the mean age of samples selected for poorer prolonged outcome (35.9) was significantly higher than for working aged patients with MHI in general (29.9). It was not, however, higher than for samples not selected for poorer prolonged outcome (36.2). This evidence, although positive, is weaker than that found for permanent PCS (18+ month's injury). Here the proportion of studies with a positive correlation was higher (75% vs. 33%). There was also a significant difference between samples selected and not selected for poorer outcome [21]. Overall the data further suggests that older age is associated with poorer chronic outcome following MHI. Its role as a potential vulnerability factor in PCS beyond the acute stages is, therefore, supported by the review.

The review also provides evidence that female gender is associated with poorer symptomatic outcome at 12–18 months after a MHI. All but one of the correlation studies

found a positive correlation in this area (and the one that did not was the smallest study). In addition the mean proportion of men in samples selected for poorer prolonged outcome (48.6%) was significantly lower than these not selected for such (63.4%). It was also lower when compared to working-age patients with MHI in general (66.7%). The proportion of correlation studies demonstrating poorer outcome with female gender was higher for this group than for those at 18+ months (83% vs. 50%) [21]. Overall, the data further suggests that female gender is associated with poorer chronic outcome. Its role as a potential vulnerability factor in PCS beyond the acute stages is, therefore, supported by the review.

These findings provide valuable prognostic information for those treating patients with MHI. The main clinical implications are for early interventions. A key feature of these is providing reassurance, including a highly positive prognosis (with a strong expectation of a complete recovery) [45]. Such prognostic information, however, has to be balanced with the fact that a small proportion of patients do not achieve such outcomes [45]. If these patients ultimately find that they have been provided with inaccurate, but confidently expressed information, it could lead to uncertainty about any future information or intervention provided. Therapeutic ruptures are likely to result and jeopardize opportunities to apply evidence-based treatments later on post-injury. Knowledge of these vulnerability factors might, therefore, be important in aiding clinical judgements about when and to what extent 'standard' early prognostic information and conceptualizations are modified. If the age factor is indicative of longer-lasting neuropathological factors, this might also imply that older patients are more likely to develop symptomatology not amenable to psychological intervention. This might explain some of the limitations in the efficacy of CBT for long-term PCS which are now emerging in the literature [46]. It might suggest that in such circumstances cognitive rehabilitation adjuncts to intervention may enhance treatment potency. For some, the psychotherapeutic aims may consequently need to be altered. A greater emphasis may need to be placed on the acceptance of, and adaptation to, some aspects of MHI sequelae, rather than an expectation of their complete amelioration.

There are clearly important and significant limitations in this kind of review. The largest of these is the very small number of relevant studies currently published in the area. The study is also limited by the lack of formal analyses of the relative strengths of the evidence or of potential publication biases. The conclusions should, therefore, be considered as provisional, pending more studies in this area being published and more rigorous analyses being applied to them.

Declaration of interest

The author reports no conflicts of interest. The author alone is responsible for the content and writing of the paper. The author confirms that he is the sole contributor to this paper and no other person has intellectual responsibilities for it. This research received no specific funding.

References

1. Tellier A, Marshall SC, Wilson KG, Smith A, Perugini M, Stiell IG. The heterogeneity of mild traumatic brain injury: Where do we stand? Brain Injury 2009;23:879–887.
2. Jennett B, Frankowski RF. The epidemiology of head injury. In: Brinkman R, editor. Handbook of clinical neurology. New York: Elsevier; 1990. pp 1–16.
3. Kraus JF, Nourjah P. The epidemiology of mild uncomplicated brain injury. Trauma 1988;28:1637–1643.
4. King NS. Mild head injury: Neuropathology, sequelae, measurement and recovery. British Journal of Clinical Psychology 1997;36: 161–184.
5. Carroll LJ, Cassidy JD, Peloso PM, Borg J, von Holst H, Holm L, Paniak C, Pepin M. Prognosis for mild traumatic brain injury: Results of the WHO collaborating centre task force on mild traumatic brain injury. Journal of Rehabilitation Medicine 2004;43: 84–105.
6. Ruff R. Two decades of advances in understanding mild traumatic brain injury. Journal of Head Trauma Rehabilitation 2005;20:5–18.
7. King NS, Kirwilliam S. The nature of permanent post concussion symptoms after mild traumatic brain injury. Brain impairment 2013;14:235–242.
8. Tsushima WT, Lum M, Geling O. Sex differences in the long-term neuropsychological outcome of mild traumatic brain injury. Brain Injury 2009;23:809–814.
9. Kant R, Smith-Seemiller L, Isaac G, Duffy J. Tc-HMPAO SPECT in persistent post-concussion syndrome after mild head injury: Comparison with MRI/CT. Brain Injury 1997;11:115–124.
10. King NS, Kirwilliam S. Permanent post-concussion symptoms following mild head injury. Brain Injury 2011;25:462–470.
11. Hiekkanen H, Kurki T, Brandstack N, Kairisto V, Tenovuo O. Association of injury severity, MRI-results and ApoE genotype with 1-year outcome in mainly mild TBI: A preliminary study. Brain injury 2009;23:396–402.
12. Culotta VP, Sementilli ME, Gerold K, Watts CC. Clinicopathological heterogeneity in the classification of mild head injury. Neurosurgery 1996;38:245–250.
13. Zetterberg H, Smith DH, Blennow K. Biomarkers of mild traumatic brain injury in cerebrospinal fluid and blood. Nature Review Neurology 2013;9:201–210.
14. Jagoda AS. Clinical policy: Neuroimaging and decision making in adult mild traumatic brain injury in the acute setting. Annals of Emergency Medicine 2008;52:714–748.
15. MacDonald CL, Johnson AM, Cooper D, Nelson EC, Werner NJ, Shimony JS, Brody DL. Detection of blast-related traumatic brain injury in US military personnel. New England Journal of Medicine 2011;364:2091–2100.
16. Lipton Ml, Gulko E, Zimmerman ME, Friedman BW, Kim M, Branch CA. Diffusion-tensor imaging implicates prefrontal axonal injury in executive function impairment following very mild traumatic brain injury. Radiology 2009;252:816–824.
17. Niogi SN, Mukherjee P. Diffusion tensor imaging in mild traumatic brain injury. Journal of Head Trauma Rehabilitation 2010;25: 241–255.
18. Levin HS, Wilde E, Troyanskaya NJ, Scheibel R, Li X. Diffusion tensor imaging of mild to moderate blast-related traumatic brain injury and its sequelae. Journal of Neurotrauma 2010;27:683–694.
19. Niemeier JP, Marwitz JH, Walker WC, Davis LC, Bushnik T, Ripley DL, Ketchum JM. Are there cognitive and neurobehavioural correlates of hormonal protection for women after TBI? Neuropsychological Rehabilitation 2013;23:363–382.
20. Rutherford MH, Merrett JD, McDonald JR. Symptoms at one year following concussion from minor head injuries. Injury 1978;10: 225–230.
21. King NS. Permanent post concussion symptoms after mild head injury: A systematic literature review of age and gender factors. Neurorehabilitation 2014;34:741–748.
22. Current Depression Among Adults - United States, 2006 and 2008. Centers for Disease Control and Prevention 2010;59:1229–1235.
23. Whitman S, Coonley-Hoganson R, Desai BT. Comparative head trauma experiences in two socioeconomically different

DOI: 10.3109/02699052.2014.954271

Chicago-area communities: A population study. American Journal of Epidemiology 1984;119:570–580.
24. Middleboe T, Andersen HS, Birket-Smith M, Friis ML. Minor head injury: Impact on general health after 1 year. A prospective follow-up study. Acta Neurologica Scandinavica 1992;85:5–9.
25. Alves W, Macciocchi SN, Barth JT. Post concussive symptoms after uncomplicated mild head injury. Journal of Head Trauma Rehabilitation 1993;8:48–59.
26. Thornhill S, Teasdale GM, Murray GD, McEwan J, Roy W, Penny K. Disability in young people and adults after head injury: A prospective cohort study. British Medical Journal 2000;320: 1631–1635.
27. Mickeviciene D, Schrader H, Obelienicne D, Surkiene D, Kunicka R, Stouner LJ, Sand T. A controlled prospective inception cohort study on post-concussion syndrome outside the medicolegal context. European Journal of Neurology 2004;11:411–419.
28. Slatyer M, Skilbeck C, Langley J, Johnson S, Thomas M, Erasmus A. Multi-domain outcome from mild traumatic brain injury in 728 subjects. Brain Injury 2008;22:7.
29. Cicerone KD, Kalmar K. Persistent post-concussion syndrome: The structure of subjective complaints after mild traumatic brain injury. Journal of Head Trauma Rehabilitation 1995;10:1–17.
30. Paniak C, Toller-Lobe G, Reynolds S, Melnyk A, Nagy J. A randomised trial of two treatments for mild traumatic brain injury: 1 year follow-up. Brain Injury 2000;14:219–226.
31. Hartlage LC, Durant-Wilson D, Patch PC. Persistent behavioural problems following mild traumatic brain injury. Archives of Clinical Neuropsychology 2001;16:561–570.
32. Emanuelson I, Andersson HE, Bjorklund R, Stalhammar D. Quality of life and post-concussion symptoms in adults after mild traumatic brain injury: A population-based study in Western Sweden. Acta Neurologica Scandinavica 2003;108:332–338.
33. Goranson TE, Graves RE, Allison D, La Freniere R. Community integration following multidisciplinary rehabilitation for traumatic brain injury. Brain Injury 2003;17:759–774.
34. Heitger MH, Jones RD, Frampton CM, Arlagh MW, Anderson TJ. Recovery in the first year after mild head injury: Divergence of symptom status and self-perceived quality of life. Journal of Rehabilitation Medicine 2007;39:612–621.
35. Stalnacke B, Elgh E, Sojka P. One-year follow-up of mild traumatic brain injury: Cognition, disability and life satisfaction of patients seeking consultation. Journal of Rehabilitation Medicine 2007;39: 405–411.
36. de Leon MB, Kirsch NL, Maio RF, Tan-Schriner CU, Millis SR, Fredriksen S, Tanner CL, Breer ML. Baseline predictors of fatigue 1 year after mild head injury. Archives of Physical Medical Rehabilitation 2009;90:956–965.
37. Roe C, Sween V, Alvsaker K, Bautz-Holter E. Post-concussion symptoms after mild traumatic brain injury: Influence of demographic factors and injury severity in a 1-year cohort study. Disability and Rehabilitation 2009;31:1235–1243.
38. Wade DT, King NS, Wenden FJ, Crawford S, Caldwell F. Routine follow up after head injury: A second randomised controlled trial. Journal of Neurology, Neurosurgery and Psychiatry 1998;65: 177–183.
39. Alves WM, Colohan ART, O'Leary TJ, Rimel RW, Jane JA. Understanding posttraumatic symptoms after minor head injury. Journal of Head Trauma Rehabilitation 1986;1:1–12.
40. Rimel RW, Giordani B, Barth JT, Boll TJ, Jane JA. Disability caused by minor head injury. Neurosurgery 1981;9:221–228.
41. Lannsjo M, Geijerstam JAF, Johansson U, Bring J, Borg J. Prevalence and structure of symptoms at 3 months after mild traumatic brain injury in a national cohort. Brain Injury 2009;23: 213–219.
42. Wade DT, Crawford S, Wenden FJ, King NS, Moss NEG. Does routine follow up after head injury help? A randomised controlled trial. Journal of Neurology, Neurosurgery and Psychiatry 1997;62:478–484.
43. Kraus JF, Black MA, Hessol N, Ley P, Rokaw W, Sullivan C, Bowers S, Knowlton S, Marshal L. The incidence of acute brain injury and serious impairment in a defined population. American Journal of Epidemiology 1984;119:186–201.
44. Strang I, MacMillan R, Jennett B. Head injuries in accident and emergency departments at Scottish hospitals. Injury 1978;10: 154–159.
45. King NS, Crawford S, Wenden FJ, Moss NEG, Wade DT. Interventions and service need following mild and moderate head injury. Clinical Rehabilitation 1997;11:13–27.
46. Potter S, Brown RG. Cognitive behavioural therapy and persistent post-concussional symptoms: Integrating conceptual issues and practical aspects of treatment. Neuropsychological Rehabilitation 2012;22:1–25.